Applicants respectfully disagree and traverse. In light of the Examiner's reasoning for rejection, Applicants believe that a clarification of the claim structure is in order. It is not required that dependent claims narrow the antecedent claim; rather, the dependent claim must incorporate its limitations, as is the case in the present claims.

35 U.S.C. §112, fourth paragraph states:

> Subject to the following paragraph, a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers. (Emphasis added).

It appears that the Examiner has not applied this statutory requirement, and has not incorporated, for example, the limitation of claims 21 and 22 into its dependent claims. For example, claim 21 recites an isolated polypeptide *comprising* a Markush group of amino acid sequences of (a)-(d). Claim 22 recites one embodiment from the Markush group, that of "amino acids 1 to 381 of SEQ ID NO: 2." Therefore, claim 22 claims an isolated polypeptide *comprising* an amino acid sequence of amino acids 1 to 381 of SEQ ID NO: 2. In other words, claim 22 *comprises* amino acids 1 to 381 of SEQ ID NO:2 and may or may not *in addition* comprise a heterologous sequence. Claim 23 recites "the polypeptide of claim 22 comprising an amino acid sequence heterologous to SEQ ID NO:2." The reason claim 23 further limits claim 22 is that claim 23 now recites that the isolated polypeptide *comprising* amino acids 1 to 381 of SEQ ID NO:2 *also comprises* a heterologous sequence. Unlike claim 22 and claim 21, claim 23 does not include sequences lacking a heterologous sequence. One common denominator in claims 21, 22, and 23 is that they all recite that amino acids 1 to 381 of SEQ ID NO:2 are a part of the subject matter claimed. In accordance with 35 U.S.C. §112, fourth paragraph, this limitation is incorporated into the dependent claims. The same is true for the remaining claims at issue.

In view of the discussion above, Applicants respectfully request that the rejection be reconsidered and withdrawn.

B. 35 U.S.C. §112, first paragraph

The rejection with respect to claims 21, 23, 25, 27-29, 33-36, 43, 44, 47, 48, 59, 61, 63-67, 72-74, 77, 78, 81, 82, 85 and 86 are maintained as allegedly lacking written description. Specifically, it is asserted that "no evidence has been provided...for which members of the genus comprising homologues or fragments of SEQ ID NO:2 comprise stimulation for cellular proliferation in vitro or in vivo." See pages 3 to 4, Paper No. 15.

Applicants respectfully disagree and traverse.

The written description requirement for a claimed genus is satisfied through disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, or by functional characteristics (see Written Description Guidelines, Fed. Reg. Vol. 66, No. 4 (January 5, 2001); MPEP §2163.05). Applicants note that the claims recite the amino acid sequence of the claimed protein (e.g., a structural characteristic) and that fragments of the invention "stimulate cellular proliferation" (e.g., a functional characteristic). As an aside, Applicants note that the claims recite that fragments of SEQ ID NO:2 have activity, based upon the Examiner's comments reiterated above, it is unclear where "homologues...compris[ing] stimulation for cellular proliferation" is recited in the claims.

Furthermore, what is conventional or well-known to one of ordinary skill in the art need not be disclosed in detail (see Written Description Guidelines, Fed. Reg. Vol. 66, No. 4 (January 5, 2001), citing *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 U.S.P.Q. at 94). Applicants note that assays for determining cell proliferation activity were well-known in the art at the time the present application was originally filed. Furthermore, polypeptide fragments of the invention are easily and routinely tested for cell proliferation activity by using such well-known cell proliferation assays.

For example, Applicants submit herewith as Exhibits A, B, and C three references illustrating assays known in the art well before the priority date of the instant application that clearly demonstrate that detection of functional peptide fragments was entirely routine (Munro and Pelham, *EMBO J.* 3:3087-3093 (1984); Pollard et al., *EMBO J.* 11:585-591 (1992); Sugiyama et al., *PNAS* 88:9603-9607 (1991)). In fact, these references were publicly available in 1984, 1991, and 1992, and are merely representative examples of the state of the art. Thus, in view of this evidence, the skilled protein chemist or molecular biologist, enlightened by the teachings of the present specification and what was known in the art at the time the application was filed, was more than capable of routinely making a large number of fragments and determining whether a given polypeptide fragment exhibits cell proliferation activity.

It is also asserted that "one of skill in the art would reasonably conclude that Applicants' were *not enabled* for the claimed genus..." (emphasis added, see page 4, Paper No. 15). Applicants note that this statement is an improper legal standard for a rejection under written description (see MPEP §2161 which states the written description requirement is separate and distinct from the enablement requirement). The proper legal standard for written description is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the

time the application was filed (see MPEP §2163.02). For the reasons discussed above, Applicants believe that this legal standard has been satisfied. Hence, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Double Patenting

Claims 22, 24, 26, 60 and 62 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly not patentably distinct over claims 37-40, 48-50 and 52 of U.S. Patent No. 5,945,300 (hereinafter '300 Patent).

Solely to facilitate prosecution and in no way acquiescing to the rejection, Applicants submit herewith a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(b). As a result, Applicants respectfully submit that the rejection has been overcome.

Rejection under 35 U.S.C. §112, second paragraph

Claims 23, 25, 27, 29, 33, 36, 40, 44, 48, 61, 63, 65, 67, 74, 78, 82 and 86 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

Applicants respectfully disagree and traverse. The term "heterologous" is a term of art with a well understood and clearly defined meaning in the art. In support of this contention, Applicants respectfully direct the Examiner's attention to Exhibit D hereto, which contains a definition of the term "homology" from a standard textbook in the art (Molecular Biology of the Cell, 3rd ed., Alberts et al., eds. Garland Publishing, Inc. (New York: 1994). Specifically, "homology" (of which "heterology" is the antonym), is defined at page G-9 as:

> Similarity in the sequence of a protein or nucleic acid or in the structure of an organ that reflects a common evolutionary origin. In contrast, analogy is a similarity in structure of function that does not reflect a common evolutionary origin.

Clearly, "heterology" means not of common, *i.e.*, of different, evolutionary origin. Thus, it is clear that the specified "heterologous" polypeptides refer to evolutionarily unrelated sequences. Therefore, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. §102

Claims 23, 25, 27, 29, 33, 36, 40, 44, 48, 61, 63, 65, 67, 74, 78, 82, and 86 under 35 U.S.C. § 102(b) as allegedly anticipated by Purchio et al. specifically, it is asserted that "Puchio

et al. teaches isolated polypeptides comprising sequences which are heterologous to SEQ ID NO:2 and the subsequences thereof." (See page 7, Paper No. 15).

Applicants respectfully disagree and traverse. To anticipate a claim, the prior art reference must teach, either explicitly or inherently, each and every element of the claim (see MPEP §2131). As discussed above, the claims at issue include the elements recited in claims 21, 34, 59 and 72. For example, in claim 21, the claim elements are amino acids 1 to 381, 2 to 381, 25 to 381 of SEQ ID NO:2 and a fragment of SEQ ID NO:2, wherein the fragment has activity. Purchio et al. does not teach, explicitly or inherently these claim elements, nor does it explicitly or inherently teach the elements contained in claims 34, 59 or 72 and therefore cannot anticipate any of the claims at issue. Again, this rejection is apparently based on the Examiner's misunderstanding discussed above, that the claims cover any heterologous sequence to SEQ ID NO:2, without the specified limitations of the antecedent claims. Therefore, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Conclusion

In view of the foregoing remarks, Applicants believe they have fully addressed the Examiner's concerns and that this application is now in condition for allowance. An early notice to that effect is urged. A request is made to the Examiner to call the undersigned at the phone number provided below if any further action by Applicants would expedite allowance of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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Enclosure
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